UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/732,520	12/07/2000	John Roderick Morrison	14390	1130

7590 08/09/2002

Attn: Leopold Presser, Esq.
Scully, Scott Murphy & Presser
400 Garden City Plaza
Garden City, NY 11530

EXAMINER	
BAKER, ANNE MARIE	
ART UNIT	**PAPER NUMBER**
1632	13

DATE MAILED: 08/09/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/732,520	MORRISON ET AL.	
	Examiner	Art Unit	
	Anne-Marie Baker, Ph.D.	1632	

-- The MAILING DATE of this communication appears on the cover she t with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 May 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-44* is/are pending in the application.

4a) Of the above claim(s) *1-21 and 33-44* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *22-32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 6 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *detailed action* .

DETAILED ACTION

The response filed May 9, 2002 (Paper No. 12) has been entered. Applicants' election, with traverse, of Group III, Claims 22-32 in Paper No. 12 is acknowledged. The elected invention is drawn to a cloned animal and a method of producing a cloned animal by nuclear transfer. The traversal is on the grounds that Group II is drawn to a method of introducing a neural stem cell into an oocyte or embryo to develop into a fetus or animal consistent with and in accordance with the claims of Group III. Applicants argue that both Group II and Group III require the same starting materials, i.e. a cell and a nucleus derived from that cell. This is not found persuasive because, contrary to Applicants' argument, the method of the invention of Group II does not require a nucleus as starting material. Rather the method of the invention of Group II requires a neural stem cell and an oocyte or embryo as starting material. This is substantially different from the method of the invention of Group III which is directed exclusively to nuclear transfer. The method of the invention of Group II is not directed to nuclear transfer. Applicants further argue that the final effect of the methods of Group II and Group III is the same. This simply is not true, as the method of the invention of Group II will produce a chimeric animal and the method of the invention of Group III will produce a cloned animal. Furthermore, the method of the invention of Group III cannot be used to produce a chimeric animal. At page 4, paragraph 1 of the response, Applicants further argue that "the methods of Groups II and III produce a genetically modified animal." This is incorrect. The method of the invention of Group II would not produce a genetically modified animal, as there is no genetic modification. Although the preamble of Claim 21, recites preparing a genetically modified animal, the method steps would not produce a genetically modified animal. The method of the invention of Group III can allegedly be used to produce animals that are or are not genetically modified. Thus, the methods of the inventions of Groups II and III differ substantially, and the methods are patentably distinct as they require different starting materials, different modes of operation, and produce different effects.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-44 are pending in the instant application.

Claims 1-21 and 33-44 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction requirement in Paper No. 12.

Accordingly, Claims 22-32 are examined herein.

Specification

The disclosure is objected to because of the following informalities:

In the table on page 32, the text underneath of "oocytes" is illegible.

In Example 12, on page 30, at line 18 and page 31, at line 14, the specification refers to "animals" but does not indicate what animal species was used in the example. Since nuclear transfer techniques vary depending on the animal species used, identification of the animal species used in the example is an essential teaching for those of skill in the art.

In the table on page 32, the first column heading reads "transfected embryonic fibroblast," but there is no guidance regarding what was used to transfect the fibroblast.

Appropriate correction is required.

Double Patenting

Applicant is advised that should Claim 31 be found allowable, Claim 32 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). Both Claims 31 and 32 depend from Claim 22. Claim 22 refers to "the resulting

embryo." The animal of Claim 31 and the animal of Claim 32 both develop from "the resulting embryo" and are therefore the same thing. Claim 31 and Claim 32 are identical in scope.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 22-32 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The claims encompass human beings and methods of making human beings which are non-statutory subject matter. Inclusion of the phrase "non-human" would be remedial.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 22-32 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are directed to a cloned animal and a method of producing a cloned animal by nuclear transfer.

The specification fails to provide an enabling disclosure for animals of the type claimed and the method of producing a cloned animal by nuclear transfer because methods of nuclear transfer, particularly new methods that have not been previously used in the art, are not routinely successful. While methods of nuclear transfer are known in the art, successful implementation of the methods is limited to the

specific methods already disclosed as being successful. Variations on the methodology are inherently unpredictable because the cellular mechanisms responsible for successful versus unsuccessful nuclear transfer are not well-understood. Some parameters affecting the success of nuclear transfer were only beginning to come to light at the time of filing of this application. Westhusin et al. (2001) disclose that a number of different variables influence the success of nuclear transfer methodology, including species, source of recipient ova, cell type of nuclei donor, treatment of donor cells prior to nuclear transfer, and the techniques employed for nuclear transfer (see abstract). Westhusin et al. state that "[a] number of different variables may affect the work effort required and the probability for producing a clone" (page 36, paragraph 3). The authors report that "[w]ithout a doubt, one of the major factors influencing the probability of cloning a specific animal is species" (page 36, paragraph 4). The authors point to a number of key steps involved in nuclear transplantation and emphasize that "[t]echniques that are required to accomplish each of these steps will vary slightly between species" and that "the efficiency of each step varies among species, ultimately affecting the ease of which a particular animal can be cloned" (page 31, paragraph 1). Of note, the authors also report in 2001 that, although the first mammal cloned from an adult cell was a sheep, no additional sheep have been reported as a result of nuclear transfer using adult cell nuclei (page 38, paragraph 4). In 2001, cloned sheep, cattle, goats, pigs, and mice had been produced by nuclear transplantation (see abstract). Cloned rats, cats, dogs, horses, and rabbits had not been made. The development of cloning methods for application to new species is highly dependent on the amount of basic information on reproduction of that species. For example, the authors report that dogs have been a challenge to clone "because many of the basic mechanisms controlling reproduction are not well understood" (page 40, paragraph 1). The reference also discusses the effect of nuclear donor cell type on cloning efficiency. The authors report that in cases where an adult animal is the target for cloning, "the cells available for use as nuclei donors may be limited" (page 40, paragraph 2). Although many different cell types have been used as donors for nuclear transfer, the lack of controlled experiments and large

number of different variables that can affect the efficiency of cloning make it unclear whether one particular cell type is superior to another for use in cloning" (page 40, paragraph 2).

The instant claims cover the use of neural stem cells as nuclear donor cells. However, neural stem cells have not been successfully used as donor cells in nuclear transfer methods. Furthermore, the instant specification does not successfully demonstrate the use of neural stem cells as nuclear donor cells to produce cloned animals.

Yin et al. (2002) discuss the effect of enucleation procedures and maturation conditions on the development of embryos reconstructed by nuclear transfer techniques. The reference reports that the potential of enucleated oocytes receiving somatic cells to develop into young *in vivo* varies among species (page 41, column 1, paragraph 1).

The references cited and the state of the art as a whole demonstrate that intensive effort is required to develop new protocols in the area of nuclear transplantation.

It is further noted that the claims recite introducing a nucleus into "an oocyte or embryo" (see Claim 22). However, the prior art clearly teaches that, in animal cloning, only enucleated oocytes are used for nuclear transfer. Embryos are not used for nuclear transfer. Furthermore, the term "embryo" encompasses a multicellular organism. There are no teachings in the prior art or the instant specification for introducing a donor cell nucleus into a multicellular embryo, or even a single-cell embryo (*i.e.*, a zygote). See, for example, Campbell et al. (1996), which clearly teaches that a donor cell nucleus is transferred to an enucleated oocyte, not an embryo. One of skill in the art would not transfer a donor cell nucleus to an embryo, because a nucleus would not survive outside of a cell. Furthermore, one of skill in the art would not expect a nucleus to survive floating around in embryo.

The specification contemplates that cells that express the telomerase catalytic component (TERT) would qualify as "continuously growing donor cells" as recited in the claims. However, the specification does not teach or contemplate any other method of producing cells that would qualify as "continuously

growing donor cells" as recited in the claims. The prior art does not offer any guidance with regard to producing cells that would constitute "continuously growing donor cells."

Although it is unclear what animal species was used in Example 12 of the instant specification, the table found under Example 13 indicates that 78 embryos (having nuclei from neural stem cells) were transferred to rats, but no live born cloned rats were produced. It is noted that, as of the filing date of this application, December 2000, the art contained no reports of cloned rats. See Westhusin et al. (2001), particularly the abstract and page 39, paragraph 4.

Given that variations on nuclear transfer methodology are not routinely successful, specific guidance must be provided to enable the instant invention. The specification must teach those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation. The claims cover the preparation of any species of animal, including animals with gene disruptions (knockout animals), by nuclear transfer methodology, but the specification does not enable the making and using of such animals. In the absence of specific guidance for using the claimed methods to produce a cloned animal, undue experimentation would have been required to practice the claimed methods to make the claimed animals.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 22-32 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 22-32 are indefinite in their recitation of "a continuously growing donor cell nucleus" because it is unclear what would constitute "a continuously growing donor cell nucleus," as a nucleus itself cannot be grown outside of a cell and the specification does not define the phrase "continuously growing."

Claims 22-32 are indefinite in their recitaion of "a continuously growing donor cell" because it is unclear what would constitute "a continuously growing donor cell." The specification does not define a "continuously growing donor cell." Thus, the metes and bounds of the claim are not clearly set forth.

Claims 22-32 are indefinite in their recitation of "[a] method of producing an animal" and "to preferably develop to a foetus or animal" because the preamble is in conflict with the conclusory statement. First, because the preamble states that the method will produce an **animal**, but the conclusory statement allows for the production of a fetus instead of animal (and distinguished from an animal, according to the claim language). Second, because the conclusory statement does not require that the embryo **actually** develop into an animal (or fetus), but rather only states that such development **"preferably"** occurs. Thus, the conclusory statement is in conflict with the preamble.

Claims 23 and 24 are indefinite in their recitation of "a continuously growing somatic cell" because it is unclear what would constitute "a continuously growing somatic cell." The specification does not define "a continuously growing somatic cell."

Claims 24 and 27 are indefinite in their recitation of "destroying" and "deleting" because it is unclear how "destroying" would be distinguished from "deleting."

Claims 24 and 27 are indefinite in their recitation of "said genetic modification" because the phrase lacks antecedent basis.

Claims 26 and 27 are indefinite in their recitation of a "TERT cell" because the specification does not define a "TERT cell" and therefore it is unclear what would constitute a "TERT cell." Thus, the metes and bounds of the claims are not clearly set forth.

Claims 29 and 30 are indefinite in their recitation of "optionally culturing the cloned cells" because the claim also recites "cloning the cleaved cells of the embryo" and "cloning" necessarily involves culturing the cells. Thus, the claim language "and optionally culturing the cloned cells" is confusing, as culturing that is necessary cannot be optional.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 28-32 are rejected under 35 U.S.C. 102(b) as being anticipated by Campbell et al. (1996).

Claim 28 is directed to an embryo produced by nuclear transfer methodology. Claim 29 is directed to a method of producing a cell line from an embryo. Claim 30 is directed to a cell line prepared from an embryo. Claim 31 is directed to an animal produced by nuclear transfer technology. Claim 32 is directed to an animal prepared from an embryo produced by nuclear transfer technology.

Claims 28, 30, 31, and 32 are product-by-process claims. Product-by-process claims are not limited to the manipulations of the recited steps, only the structure implied by the steps. The patentability of a product does not depend on its method of production. See MPEP 2113. Thus, the claims read on animals, embryos, and cell lines disclosed in the prior art, as discussed below.

Campbell et al. (1996) disclose sheep produced by nuclear transfer. Such an animal would not be structurally different from the animals claimed in Claims 31 and 32. The reference also discloses a cell line established from cells isolated from sheep embryos. This cell line, designated TNT4, was used as the nuclear donor cell. Such a cell line would not be structurally different from a cell line as claimed in Claim 30. The reference also discloses reconstructed sheep embryos (p. 64, column 2, paragraph 3 through page 65, column 1). Such an embryo would not be structurally different from an embryo as claimed in Claim 28.

Campbell et al. also discloses a method for producing a cell line from an embryo. Cells were isolated from sheep embryos and were cultured for 6 to 13 passages to produce an established cell line (see abstract). This embryo-derived cell line was designated TNT4.

Thus, the claimed compositions and method were disclosed in the prior art.

Claims 29 and 30 are rejected under 35 U.S.C. 102(b) as being anticipated by Evans and Kaufman (1981).

Claim 29 is directed to a method of producing a cell line from an embryo. Claim 30 is directed to a cell line prepared from an embryo.

Claim 30 is a product-by-process claim. Product-by-process claims are not limited to the manipulations of the recited steps, only the structure implied by the steps. The patentability of a product does not depend on its method of production. See MPEP 2113. Thus, the claim reads on cell lines disclosed in the prior art, as discussed below.

Evans and Kaufman (1981) disclose a method for producing a cell line from an embryo. Cells were isolated from mouse embryos and cultured to establish a cell line designated as EK cells, now known as ES cells. Although Claim 29 recites that the embryo is obtained using nuclear transfer technology to reconstruct an embryo, after several cell divisions the embryo that develops from a reconstructed embryo is not structurally different from a normal embryo, such as a normal mouse embryo. Thus, the embryo used in Claim 29 is equivalent to any embryo isolated from any normal animal. Thus, the cell line produced from the embryo is equivalent to any embryo-derived cell line.

Thus, the claimed method of producing a cell line and the claimed cell line are disclosed in the prior art.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne-Marie Baker whose telephone number is (703) 306-9155. The examiner can normally be reached Monday through Thursday and alternate Fridays from 10:00 AM to 7:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached on (703) 305-4051. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-8724.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the patent analyst, Dianiece Jacobs, whose telephone number is (703) 305-3388.

Anne-Marie Baker, Ph.D.

Anne-Marie Baker

ANNE-MARIE BAKER
PATENT EXAMINER